Complete Summary

GUIDELINE TITLE

2002 national guideline on the management of non-gonococcal urethritis.

BIBLIOGRAPHIC SOURCE(S)

Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline on the management of non-gonococcal urethritis. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [31 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Non-gonococcal urethritis (NGU):

- Acute non-gonococcal urethritis
- Persistent/recurrent non-gonococcal urethritis

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Infectious Diseases
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present a national guideline for the management of non-gonococcal urethritis

TARGET POPULATION

Men in the United Kingdom with non-gonococcal urethritis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Gram stained urethral smear
2. Gram stained preparation from a first pass urine (FPU) specimen
3. Leucocyte esterase activity on first pass urine specimen

Treatment/Management

1. Patient education
2. Doxycycline or azithromycin
3. Erythromycin, or ofloxacin
4. Erythromycin plus metronidazole
5. Partner(s) assessment and treatment
6. Follow up

MAJOR OUTCOMES CONSIDERED

Microbiological cure rate

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developers performed Medline searches for 1970 to the present using keywords "Non-gonococcal urethritis", "nongonococcal urethritis", "non-specific urethritis," "NGU", "NSU". The guideline developers also searched the Cochrane Library for 1970 to the present using keywords "Non-gonococcal urethritis", "nongonococcal urethritis", "non-specific urethritis", "NGU", "NSU".

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence:

Ia

- Evidence obtained from meta-analysis of randomised controlled trials

Ib

- Evidence obtained from at least one randomised controlled trial

IIa

- Evidence obtained from at least one well designed controlled study without randomisation

IIb

- Evidence obtained from at least one other type of well designed quasi-experimental study

III

- Evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies, and case control studies

IV

- Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The revision process commenced with authors being invited to modify and update their 1999 guidelines. These revised versions were posted on the website for a 3 month period and comments invited. The Clinical Effectiveness Group and the authors concerned considered all suggestions and agreed on any modifications to be made.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations:

A (Evidence Levels Ia, Ib)

- Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B (Evidence Levels IIa, IIb, III)

- Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

C (Evidence Level IV)

- Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities.
- Indicates absence of directly applicable studies of good quality.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial versions of the guidelines were sent to the following for review:

- Clinical Effectiveness Group (CEG) members
- Chairs of UK Regional GU Medicine Audit Committees who had responded to an invitation to comment on the guidelines
- Chair of the Genitourinary Nurses Association (GUNA)
- President of the Society of Health Advisers in Sexually Transmitted Diseases (SHASTD)

- Clinical Effectiveness Committee of the Faculty of Family Planning and Reproductive Health Care (FFP).

Comments were relayed to the authors and attempts made to reach a consensus on points of contention with ultimate editorial control resting with the Clinical Effectiveness Group. Finally, all the guidelines were ratified by the councils of the two parent societies.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Levels of evidence (I-IV) and grades of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Diagnosis

The diagnosis of urethritis must be confirmed by demonstrating polymorphonuclear leucocytes (PMNLs) in the anterior urethra. This can be by means of:

(i) a Gram stained urethral smear containing $\geq$5 polymorphonuclear leucocytes (PMNL) per high power (x 1000) microscopic field (averaged over five fields with greatest concentration of polymorphonuclear leucocytes) (Swartz et al., 1978)

and/or

(ii) a Gram stained preparation from a first pass urine (FPU) specimen, containing $\geq$10 polymorphonuclear leucocytes per high power (x 1000) microscopic field (averaged over five fields with greatest concentration of polymorphonuclear leucocytes).

- Either test can be used: Both tests will identify cases missed by the other. (Janier et al., 1995)
- The quality of the smear is heavily dependent on how the smear is taken.
- Either a 5 mm plastic loop or cotton tipped swab can be used. There are no published data comparing the two, but the former appears to be less traumatic to the patient.
- Positive leucocyte esterase activity on first pass urine specimen correlates with non-gonococcal urethritis (NGU) and is considered diagnostic by some authorities. (Munday, Altman, & Taylor-Robinson, 1981) However, it does not have adequate sensitivity to be considered a reliable rapid diagnostic test for non-gonococcal urethritis. (Centers for Disease Control and Prevention, 1998; Patrick, Rekart, & Knowles, 1994)

The sensitivity of the above tests is affected by the period since last passing urine. The optimum time to ensure a definite diagnosis in a symptomatic man is not known. Four hours is conventional.

Symptomatic patients in whom no urethritis is detected initially, should be re-tested having held their urine overnight. Empirical treatment of these patients is

not recommended unless they have an observable mucopurulent/purulent discharge or are at high risk of infection and are unlikely to return for repeat evaluation.

Investigations

- All patients should have a urethral culture for Neisseria gonorrhoeae.
- Chlamydia trachomatis should also be sought (see the related guideline titled 2002 Clinical Effectiveness Guideline for the Management of Chlamydia Trachomatis Genital Tract Infection).
- Urinalysis of the mid-stream urine (MSU) specimen may be useful, using a dipstick which contains leucocyte esterase and nitrites, in addition to testing for blood, protein, and glucose. (Fraser et al., 1995) In positive cases a mid-stream urine specimen should be sent for microscopy and culture.
- Formerly, the two glass test was used to diagnose non-gonococcal urethritis and to differentiate it from urinary tract infection. This test, however, has an unacceptably low specificity and sensitivity. (Flanagan et al., 1989)

Management

General advice

The following should be discussed and clear written information provided:

- A detailed explanation of what non-gonococcal urethritis is and what causes it, with particular emphasis on the long term implications for the health of the patient and his partner
- Side effects of treatment and importance of complying fully with it
- The importance of the sexual partner(s) being evaluated and treated
- Advised to abstain from sexual intercourse until he has completed therapy and his partner(s) have been treated
- Advice on safer sex

Treatment

Treatment should be initiated as soon as the diagnosis is made. Ideally treatment should be effective (microbiological cure rate for Chlamydia trachomatis >95%), easy to take (not more than twice daily), with a low side effect profile, and cause minimal interference with daily lifestyle. In general, regimens which are effective against Chlamydia trachomatis are also effective in non-gonococcal urethritis. Assessing treatments is problematic as there are methodological difficulties in defining efficacy.

Recommended regimens (Grade of Recommendation A)

- Doxycycline 100 mg twice a day for 7 days (Level of Evidence Ib)

or

- Azithromycin 1 g orally in a single dose (Level of Evidence Ib).

Alternative regimens (Grade of Recommendation A)

- Erythromycin 500 mg twice daily for 14 days (Level of Evidence Ib)

or

- Ofloxacin 200 mg twice a day or 400 mg once a day for 7 days (Level of Evidence Ib)

Compliance with therapy

While single dose therapy has the advantage of improved compliance, azithromycin has not been shown to be more effective in clinical studies than doxycycline. There is evidence to show that in general compliance is improved where there is a positive therapeutic relationship between the patient and the doctor (see the related guideline titled 2002 Clinical Effectiveness Guideline for the Management of Chlamydia Trachomatis Genital Tract Infection).

In those patients with erratic healthcare seeking behaviour, in whom compliance is anticipated to be poor, an argument can be made for prescribing azithromycin (see the related guideline titled 2002 Clinical Effectiveness Guideline for the Management of Chlamydia Trachomatis Genital Tract Infection).

Sexual Contacts/Partners

- All sexual partners at risk should be assessed and offered epidemiological treatment, maintaining patient confidentiality. The duration of "look back" is arbitrary; 4 weeks is suggested for symptomatic men and up to 6 months for asymptomatic men.
- The treatment regimen used should be as detailed for uncomplicated Chlamydia trachomatis infection.
- If Chlamydia trachomatis or Neisseria gonorrhoeae are detected it is particularly important to ensure that all sexual partner(s) potentially at risk have been notified.
- Details of all contacts should be obtained at the first visit. Consent should also be obtained to contact either the patient or his partners if tests for Chlamydia trachomatis or Neisseria gonorrhoeae are found to be positive. This insures that if the index patient does not reattend, he can be contacted and/or provider referral can be initiated for sexual contacts.
- Female contacts of men with chlamydial urethritis should be treated regardless of the results of chlamydia isolation (Ib).
- Concurrent treatment of the sexual partner of men with chlamydia negative non-gonococcal urethritis may result in an improved response in some patients, and a possible reduction in female morbidity (III). This has not been evaluated in randomised prospective studies. Non-gonococcal urethritis cohort studies have looked at the effect on response of urethritis and have produced conflicting conclusions. (Evans, 1978; Bowie et al., 1981) There are reports of patients with persistent or recurrent urethritis being cured only after their sexual partner received appropriate treatment. (Ford & Henderson, 1976) There is evidence that at least some men with "chlamydia negative" non-gonococcal urethritis have partners who are chlamydia-positive. (Singh & Blackwell, 1994; Tait, 2000) In addition, asymptomatic Chlamydia

trachomatis infection can be cleared without treatment, whether these men have non-gonococcal urethritis is unknown. (Morre et al., 2000)

Follow Up for Patients with Non-gonococcal Urethritis

This is an important part of the management of non-gonococcal urethritis, and should take place 2 weeks after initiating therapy. However, some patients may not return, emphasising the importance of the initial consultation. Follow up has a number of objectives including:

- following up partner notification
- reinforcing health education
- providing reassurance
- assessment of treatment compliance and efficacy
- repeat urethral smear and first pass urine specimen to look for persistent urethritis only if patient is symptomatic or has a urethral discharge on examination (test of cure)

Persistent/Recurrent Non-gonococcal Urethritis

There is no consensus of opinion on either diagnosis or management of this condition. Its aetiology is probably multifactorial. (Horner et al., 2001; Horner & Coker, 1999; Bowie et al., 1981; Horner et al., 1997; Munday, 1985) It occurs in 20-60% of men treated for acute non-gonococcal urethritis (Horner et al., 2001; Horner & Coker, 1999; Bowie et al., 1981; Munday, 1985; Hay et al., 1992; Romanowski et al., 1993; Shahmanesh, 1994) and it is unknown whether patients who have asymptomatic urethritis at follow up are more likely to have an acute relapse than those with no urethritis at follow-up. One study recently defined chronic non-gonococcal urethritis as persistent or recurrent urethritis occurring 30 to 92 days following treatment of acute non-gonococcal urethritis. (Horner et al., 2001) They argue that this is clinically pragmatic.

Persistent chlamydial infection is only rarely detected, providing the patient and partner(s) have complied with treatment. (Horner & Coker, 1999; Horner et al., 1997; Munday, 1985; Hay et al., 1992) There is evidence that ureaplasmas and Mycoplasma genitalium may be important in the aetiology of chronic non-gonococcal urethritis with either symptoms or signs. (Horner et al., 2001)

There is no evidence that female partners of men with persistent/recurrent non-gonococcal urethritis are at increased risk of pelvic inflammatory disease.

Diagnosis of persistent/recurrent non-gonococcal urethritis

- Urethral smear and first pass urine specimen to evaluate polymorphonuclear leucocytes (as for non-gonococcal urethritis)
- If patient symptomatic with no objective evidence of non-gonococcal urethritis, an early morning smear should be undertaken and if negative, reassure.

Management of persistent/recurrent non-gonococcal urethritis

- Ensure patient has completed initial course of therapy. If not, consider represcribing initial treatment
- Ensure sexual partner(s) have been treated and re-infection is not a possible cause
- If patient has no signs or symptoms consider reassurance.

Recommended regimens (Grade of Recommendation C)

Patient symptomatic or an observable discharge present (Horner et al., 2001; Horner et al., 1997; Hay et al., 1992; Hooton et al., 1990)

- Erythromycin 500 mg four times a day for two week

plus

- Metronidazole 400 mg twice a day for five days

Continuing symptoms

There is only limited evidence on how best to manage patients who either remain symptomatic following a second course of treatment or who have frequent recurrences after treatment.

- Erythromycin 500 mg four times daily for 3 weeks may help. (Hooton et al., 1990)
- Urological investigation is usually normal unless the patient has urinary flow problems. (Krieger, Hooton & Brust, 1988)
- Chronic abacterial prostatitis (see the related guideline titled 2002 National Guideline for the Management of Prostatitis) and psychosexual causes should be considered in the differential diagnosis. (Horner & Coker, 1999; Hooton et al., 1990; Krieger, Hooton, & Brust 1988; Wong et al., 1988)
- There is no evidence to suggest that patients with microscopic urethritis but who have no signs or symptoms after two courses of treatment are persistently infected. They should be reassured.
- Re-treatment of the sexual partner may be helpful in recurrent urethritis as it may be due to re-infection. This has not been evaluated in clinical studies.
- For men with persistent urethritis, there is no evidence that re-treatment of an appropriately treated sexual partner is beneficial.

Definitions:

Levels of Evidence:

Ia

- Evidence obtained from meta-analysis of randomised controlled trials

Ib

- Evidence obtained from at least one randomised controlled trial

IIa

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C (Evidence Level IV)

- Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities.
- Indicates absence of directly applicable studies of good quality.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is graded and identified for select recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis, treatment and management of non-gonococcal urethritis

POTENTIAL HARMS

Not stated

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Clinical Effectiveness Group reminds the reader that guidelines in themselves are of no use unless they are implemented systematically. The following auditable outcome measures are provided:

- Compliance with clinical standards of care
- Partner notification
- Patient's knowledge of non-gonococcal urethritis and how to reduce the risk of acquiring it

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline on the management of non-gonococcal urethritis. London: Association for Genitourinary Medicine (AGUM),

Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [31 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Aug (revised 2002)

GUIDELINE DEVELOPER(S)

Association for Genitourinary Medicine - Medical Specialty Society
Medical Society for the Study of Venereal Diseases - Disease Specific Society

SOURCE(S) OF FUNDING

Not stated

GUIDELINE COMMITTEE

Clinical Effectiveness Group (CEG)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Dr Patrick J Horner and Dr Mohsen Shahmanesh

Clinical Effectiveness Group (CEG) Members: Keith Radcliffe (Chairman); Imtyaz Ahmed-Jushuf; Jan Welch; Mark FitzGerald; Janet Wilson

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Conflicts of interest: None

GUIDELINE STATUS

This is the current release of the guideline. This guideline updates a previously released version.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in HTML format from the Association for Genitourinary Medicine (AGUM) Web site. Also available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following background documents are available:

- UK national guidelines on sexually transmitted infections and closely related conditions. Introduction. Sex Transm Infect 1999 Aug;75(Suppl 1):S2-3. Electronic copies: Available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases (MSSVD) Web site.
- Revised UK national guidelines on sexually transmitted infections and closely related conditions 2002. Sex Transm Infect 2002;78:81-2

Print copies: For further information, please contact the journal publisher, BMJ Publishing Group.

The following related guidelines are available:

- 2002 clinical effectiveness guideline for the management of chlamydia trachomatis genital tract infection. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. See the National Guideline Clearinghouse (NGC) summary.
- 2002 national guideline for the management of prostatitis. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. See the NGC summary.

Electronic copies: Available in HTML format from the Association for Genitourinary Medicine (AGUM) Web site. Also available in Portable Document Format (PDF) from the Medical Society for the Study of Venereal Diseases Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 15, 2000. The information was verified by the guideline developer on October 13, 2000. This summary was updated by ECRI on June 24, 2002.

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